

REMARKS/ARGUMENTS

Claims 1-162, 167, 188, and 205-265 are pending. Claims 163-166, 168-187, and 189-204 have been canceled without prejudice or disclaimer. As noted in the Office Action, pending claims 249-263 have been renumbered as claims 248-262 in view of an inadvertent clerical error (*i.e.*, a missing claim 248) in the application as filed. Accordingly, renumbered claims 255, 256, and 262 have been amended to correct claim dependency, as requested in the Office Action. Claims 263-265 have been added and are directed to preferred 1,4-benzothiazepine and 1,5-benzothiazepine substituents, which are described in the specification, *e.g.*, at paragraphs [39], [40], [41], [46], [106], and [142] (*see* pp. 7-9, 18, and 24-37). Accordingly, no new matter is added.

Claim amendments follow the Revised Amendment Practice under 37 CFR § 1.121 (effective July 30, 2003) rather than the previous practice described on pages 2-3 of the Office Action.

Applicants note with appreciation that claims 238-240 and 242-249 are allowable, save for being written in independent form, and that claims 226-299 and 231-236 are allowed.

Previous Rejections of Claims 1-225, 230, 237-253, and 256-260 under 35 U.S.C. § 112, ¶ 2

For convenience, Applicants' remarks below are provided in lettered paragraphs using the corresponding numbering scheme of the paragraphs in the Office Action.

d) In response to the rejection of claims 1-225, 250-253, and 256-260, for reciting "alkylaminoalkyl", Applicants have amended claims 1-3, 8-10, 29-31, 36-38, 75-77, 82-84, 121, 122, 125, 141, 142, 145, and 205 to replace "alkylammoniumalkyl" with "alkylaminoalkyl",

indicating an amino radical that is substituted with two alkyl radicals. According to the definition of “alkylammoniumalkyl” given in paragraph [569] of the specification (*see* p. 156), “alkylammoniumalkyl” includes di-substituted amino groups, with one of the alkyl substituents bonded to the parent molecule. Accordingly, no new matter is added.

Applicants respectfully submit that the rejections with respect to claims 163 and 184 are rendered moot by the cancellation of these claims. Moreover, the amendments noted above were incorporated into claims 167 and 188, which have now been rewritten in independent form to include all of the limitations of canceled base claims 163 and 184, respectively.

Withdrawal of this rejection is respectfully requested.

o) In response to the rejection of claims 14, 42, 88, 128, 148, and their dependent claims, Applicants have amended claims 14, 42, and 88 to explicitly show that, in the penultimate structure shown for the R¹⁹ moieties, the nitrogen atom adjacent to the sulfonyl has a third bond to a hydrogen. Applicants have amended claims 128 and 148 to explicitly show that, in the penultimate structures shown for the R²⁴ and R²⁹ moieties, respectively, the nitrogen atom adjacent to the sulfonyl has a third bond to a hydrogen.

In addition, claims 3, 31, 77, 122, and 142 were amended, in the amendment filed on April 2, 2003, to recite the structure at issue. Accordingly, Applicants have amended claims 3, 31, and 77 to explicitly show that, in the penultimate structure shown for the R¹⁹ moieties, the nitrogen atom adjacent to the sulfonyl has a third bond to a hydrogen. Applicants have amended claims 122 and 142 to explicitly show that, in the penultimate structures shown for the R²⁴ and R²⁹ moieties, respectively, the nitrogen atom adjacent to the sulfonyl has a third bond to a hydrogen.

Withdrawal of this rejection is respectfully requested.

r) In response to the rejection of claims 29, 75 and their dependent claims, Applicants have amended these claims to replace “ $-\text{O}(\text{CH}_2)_{1-4}\text{NR}'\text{R}''\text{R}'''$ ” with “ $-\text{O}(\text{CH}_2)_{1-4}\text{N}^+\text{R}'\text{R}''\text{R}'''\text{A}^-$ ”, explicitly showing a positive charge on the nitrogen atom that is balanced by A^- , defined in the claims as a pharmaceutically acceptable anion. Applicants respectfully submit that one of ordinary skill in the art would readily understand this tetravalent nitrogen atom to be both positively charged and balanced by a pharmaceutically acceptable anion. For example, an analogous moiety explicitly showing both the positive charge and charge-balancing pharmaceutically acceptable anion is given in the last line of paragraph [904] of the specification (*see* p. 388). Numerous other moieties show N^+ , balanced by A^- throughout the specification. Accordingly, no new matter is added.

Withdrawal of this rejection is respectfully requested.

u) In response to the rejection of claim 141 and its dependent claims, Applicants have amended this claim to explicitly show a hydrogen atom, to which the ring nitrogen atom on the core structure of Formula V is bonded. Applicants respectfully submit that one of ordinary skill in the art would readily understand that this trivalent nitrogen atom, in the absence of any other third substituent shown, is bonded to hydrogen. In the specification, numerous compounds within the scope of Formula V show this hydrogen atom. *See, e.g.*, Example 3, paragraph [621], at p. 164 of the specification. Accordingly, no new matter is added.

Withdrawal of this rejection is respectfully requested.

w-y) Applicants respectfully submit that the rejections of claim 169 are rendered moot by the cancellation of this claim. Withdrawal of this rejection is respectfully requested.

z-ab) Applicants respectfully submit that the rejections of claim 190 are rendered moot by the cancellation of this claim.

Withdrawal of this rejection is respectfully requested.

ac) In response to the rejection of claim 211 and its dependent claims, Applicants have amended this claim to explicitly show hydrogen atoms bonded to nitrogen atoms in many of the structures (excluding those deleted in view of rejections noted in paragraphs **ad** and **ae**) where these nitrogen atoms are substituted in alkyl carbon atom chains. Applicants respectfully submit that one of ordinary skill in the art, especially in view of the specification, would readily understand that these trivalent nitrogen atoms, in the absence of any other third substituent shown, are bonded to hydrogen. For example, claim 206 (*see* p. 534), from which claim 211 depends, recites the R^{32} moiety “ $-N(H)-X-R^{33}$ ”, which explicitly shows the hydrogen atom bonded to the left-hand nitrogen in the claim 211 structures. Accordingly, no new matter is added.

Withdrawal of this rejection is respectfully requested.

ad-ae) In response to the rejection of claim 211 and its dependent claims, and in the interest of furthering prosecution, Applicants have amended this claim to delete the structures that the Office Action contends are not within the scope of R^{33} . These structures are now recited as R^{30} , R^{31} , and R^{34} structures (with all nitrogen substituents explicitly shown) in new claim 265, which depends from claim 205. Applicants submit that the definitions of R^{30} , R^{31} , and R^{34} in claim 205 include these structures.

Withdrawal of this rejection is respectfully requested.

af) In response to the rejection of claim 230 and its dependent claims, Applicants

have amended this claim to explicitly show hydrogen atoms bonded to nitrogen atoms in many of the structures (excluding those deleted in view of rejections noted in paragraphs **ag** and **ah**) where these nitrogen atoms are substituted in alkyl carbon atom chains. Applicants respectfully submit that one of ordinary skill in the art, especially in view of the specification, would readily understand that these trivalent nitrogen atoms, in the absence of any other third substituent shown, are bonded to hydrogen. For example, claim 227 (*see* p. 543), from which claim 230 depends, recites the R^{32} moiety “-N(**H**)-X- R^{33} ”, which explicitly shows the hydrogen atom bonded to the left-hand nitrogen in the claim 230 structures. Accordingly, no new matter is added.

Withdrawal of this rejection is respectfully requested.

ag-ah) In response to the rejection of claim 230 and its dependent claims, and in the interest of furthering prosecution, Applicants have amended this claim to delete the structures that the Office Action contends are not within the scope of R^{33} . These structures are now recited as R^{30} , R^{31} , and R^{34} structures (with all nitrogen substituents explicitly shown) in new claim 266, which depends from claim 226. Applicants submit that the definitions of R^{30} , R^{31} , and R^{34} in claim 226 include these structures.

Withdrawal of this rejection is respectfully requested.

ag 2nd) In response to the rejection of claim 237 and its dependent claims, Applicants have amended this claim to explicitly show a hydrogen atom, to which the ring nitrogen atom on the core structure of Formula IX is bonded. Applicants respectfully submit that one of ordinary skill in the art would readily understand that this trivalent nitrogen atom, in the absence of any other third substituent shown, is bonded to hydrogen. In the specification, numerous compounds

within the scope of Formula IX show this hydrogen atom. *See, e.g.*, paragraph [868], at p. 235 of the specification. Accordingly, no new matter is added.

Withdrawal of this rejection is respectfully requested.

ah 2nd) In response to the rejection of claim 241 and its dependent claims, Applicants have amended this claim to explicitly show hydrogen atoms bonded to nitrogen atoms in many of the structures (excluding those deleted in view of rejections noted in paragraphs **ai** and **aj**) where these nitrogen atoms are substituted in alkyl carbon atom chains. Applicants respectfully submit that one of ordinary skill in the art, especially in view of the specification, would readily understand that these trivalent nitrogen atoms, in the absence of any other third substituent shown, are bonded to hydrogen. For example, claim 238 (*see* p. 551), from which claim 241 depends, recites the R³² moiety “-N(H)-X-R³³”, which explicitly shows the hydrogen atom bonded to the left-hand nitrogen in the claim 241 structures. Accordingly, no new matter is added.

Withdrawal of this rejection is respectfully requested.

ai-aj) In response to the rejection of claim 241 and its dependent claims, and in the interest of furthering prosecution, Applicants have amended this claim to delete the structures that the Office Action contends are not within the scope of R³³. These structures are now recited as R³⁰, R³¹, and R³⁴ structures (with all nitrogen substituents explicitly shown) in new claim 267, which depends from claim 237. Applicants submit that the definitions of R³⁰, R³¹, and R³⁴ in claim 237 include these structures.

Withdrawal of this rejection is respectfully requested.

Rejection of Claims 1-9, 14-37, 42-83, 88-124, 128-144, 148-225, 250-253, and 256-260 under

35 U.S.C. § 112, ¶ 1

Claims 1-9, 14-37, 42-83, 88-124, 128-144, 148-225, 250-253, and 256-260 have been rejected under 35 U.S.C. § 112, ¶ 1 as containing subject matter which was not described in the specification. In particular, the Office Action asserts that, “The amendment with respect to the definition of the substituents on the alkyl, haloalkyl...and polyether radicals of R^{13} , R^{14} , and R^{15} where the list of moieties includes the moiety ‘ $-N^+R^9R^{11}R^{12}A^-$ ’ ...is not described in the specification for the genus.”

In response, Applicants have amended claims 1–3, 8, 9, 29-31, 36, 37, 75-77, 82, 83, 121, 122, 141, 142, and 205 to recite “ $-N^+R^9R^{11}R^{12}A^-$ ” as a substituent for alkyl, polyether, aryl, quaternary heterocyclyl, arylalkyl, heterocyclylalkyl, quaternary heterocyclylalkyl, alkylheterocyclylalkyl, and alkylaminoalkyl. Support for this amendment is found in the specification, *e.g.*, in paragraphs [129] and [131] (*see* p. 22-23) and in paragraphs [252] and [254] (*see* p. 54).

Applicants respectfully submit that the rejections with respect to claims 163 and 184 are rendered moot by the cancellation of these claims. Moreover, the amendments noted above were incorporated into claims 167 and 188, which have now been rewritten in independent form to include all of the limitations of canceled base claims 163 and 184, respectively.

Withdrawal of this rejection is respectfully requested.

Rejection of Claims 1-225, 250-253, and 256-260 under 35 U.S.C. § 112, ¶ 1

Claims 1-225, 250-253, and 256-260 have been rejected under 35 U.S.C. § 112, ¶ 1 as containing subject matter which was not described in the specification. In particular, the Office Action asserts that, “The amendment with respect to the definition of the substituents on the alkyl, cycloalkyl...polyether, and acyloxy radicals of R⁶, where the list of moieties includes the moiety ‘-N⁺R⁹R¹¹R¹²A’ ...is not described in the specification for the genus.”

In response, Applicants have amended claims 1 and 75 to delete “-N⁺R⁹R¹¹R¹²A” from the definition of substituents for R⁶ radicals.

Withdrawal of this rejection is respectfully requested.

New Rejections of Claims 1-225, 250-253, and 256-260 under 35 U.S.C. § 112, ¶ 2

For convenience, Applicants’ remarks below are provided in lettered paragraphs using the corresponding numbering scheme of the paragraphs in the Office Action.

a) In response to the rejection of claim 1 and its dependent claims as being vague and indefinite for reciting “-P¹³R¹⁴” in the list of substituents for the quaternary heterocyclyl moiety of R⁶, Applicants have amended claim 1 to replace “-P¹³R¹⁴” with “-PR¹³R¹⁴” and thereby correct the typographical error.

Withdrawal of this rejection is respectfully requested.

b-c) In response to the rejection of claim 9 and its dependent claims as being vague and indefinite for including a slash mark through a hyphen in two locations, Applicants have amended claim 9 to delete this matter and thereby correct these typographical errors.

Withdrawal of this rejection is respectfully requested.

d-e) In response to the rejection of claims 10 and 11 as lacking antecedent basis for “carboxyalkylheterocycle” in the definition of R^9 and R^{10} , Applicants have amended claims 1, 2, and 3, from which claims 10 and 11 depend, to insert “carboxyalkylheterocycle” in this definition. Support for these amendments is found throughout the specification, *e.g.*, in paragraph [139] (see p. 24). Accordingly, no new matter is added.

Withdrawal of this rejection is respectfully requested.

f) In response to the rejection of claim 29 and its dependent claims as being vague and indefinite for reciting “ $-P^9R^{10}$ ” in the list of substituents for the R^6 moieties, Applicants have amended claim 29 to replace “ $-P^9R^{10}$ ” with “ $-PR^9R^{10}$ ” and thereby correct the typographical error.

Withdrawal of this rejection is respectfully requested.

g) In response to the rejection of claim 29 and its dependent claims as being vague and indefinite for reciting “ $-P^{13}R^{14}$ ” in the list of substituents for the quaternary heterocyclyl moiety of R^6 , Applicants have amended claim 29 to replace “ $-P^{13}R^{14}$ ” with “ $-PR^{13}R^{14}$ ” and thereby correct the typographical error.

Withdrawal of this rejection is respectfully requested.

h-i) In response to the rejection of claims 38 and 39 as lacking antecedent basis for “carboxyalkylheterocycle” in the definition of R^9 and R^{10} , Applicants have amended claims 29, 30, and 31, from which claims 38 and 39 depend, to insert “carboxyalkylheterocycle” in this definition. Support for these amendments is found throughout the specification, *e.g.*, in paragraph [139] (see p. 24). Accordingly, no new matter is added.

Withdrawal of this rejection is respectfully requested.

j) In response to the rejection of claim 75 and its dependent claims as being vague and indefinite for reciting “-P¹³R¹⁴” in the list of substituents for the quaternary heterocyclyl moiety of R⁶, Applicants have amended claim 75 to replace “-P¹³R¹⁴” with “-PR¹³R¹⁴” and thereby correct the typographical error.

Withdrawal of this rejection is respectfully requested.

k-l) In response to the rejection of claims 84 and 85 as lacking antecedent basis for “carboxyalkylheterocycle” in the definition of R⁹ and R¹⁰, Applicants have amended claims 75, 76, and 77, from which claims 84 and 85 depend, to insert “carboxyalkylheterocycle” in this definition. Support for these amendments is found throughout the specification, *e.g.*, in paragraph [139] (see p. 24). Accordingly, no new matter is added.

Withdrawal of this rejection is respectfully requested.

m) In response to the rejection of claim 125 as lacking antecedent basis for “carboxyalkylheterocycle” in the definition of R⁹ and R¹⁰, Applicants have amended claims 121 and 122, from which claim 125 depends, to insert “carboxyalkylheterocycle” in this definition. Support for these amendments is found throughout the specification, *e.g.*, in paragraph [139] (see p. 24). Accordingly, no new matter is added.

Withdrawal of this rejection is respectfully requested.

n) In response to the rejection of claim 145 as lacking antecedent basis for “carboxyalkylheterocycle” in the definition of R⁹ and R¹⁰, Applicants have amended claims 141 and 142, from which claim 145 depends, to insert “carboxyalkylheterocycle” in this definition. Support for these amendments is found throughout the specification, *e.g.*, in paragraph [139] (see p. 24). Accordingly, no new matter is added.

Withdrawal of this rejection is respectfully requested.

o) Applicants respectfully submit that the rejection of claim 163 and its dependent claims as being vague and indefinite for reciting “-P⁹R¹⁰” in the list of substituents for the R³⁴ moieties (rather than the R⁶ moieties as stated in the Office Action) is rendered moot by the cancellation of this claim. Moreover, claim 167, which has now been rewritten in independent form to include all of the limitations of canceled base claim 163, recites “-PR⁹R¹⁰”, instead of “-P⁹R¹⁰” to correct the typographical error noted in the Office Action.

Withdrawal of this rejection is respectfully requested.

p) Applicants respectfully submit that the rejection of claim 163 and its dependent claims as being vague and indefinite for reciting “-P¹³R¹⁴” in the list of substituents for the quaternary heterocyclyl moiety of R³⁴ (rather than the quaternary heterocyclyl moiety of R⁶ as stated in the Office Action), is rendered moot by the cancellation of this claim. Moreover, claim 167, which has now been rewritten in independent form to include all of the limitations of canceled base claim 163, recites “-PR¹³R¹⁴”, instead of “-P¹³R¹⁴” to correct the typographical error noted in the Office Action.

Withdrawal of this rejection is respectfully requested.

q) Applicants respectfully submit that the rejection respect to claim 166 for failing to end with a period is rendered moot by the cancellation of this claim.

Withdrawal of this rejection is respectfully requested.

r) Applicants respectfully submit that the rejection of claim 184 and its dependent claims as being vague and indefinite for reciting “-P⁹R¹⁰” in the list of substituents for the R³⁴ moieties (rather than the R⁶ moieties as stated in the Office Action) is rendered moot by the

cancellation of this claim. Moreover, claim 188, which has now been rewritten in independent form to include all of the limitations of canceled base claim 184, recites “PR⁹R¹⁰”, instead of “P⁹R¹⁰” to correct the typographical error noted in the Office Action.

Withdrawal of this rejection is respectfully requested.

s) Applicants respectfully submit that the rejection of claim 184 and its dependent claims as being vague and indefinite for reciting “P¹³R¹⁴” in the list of substituents for the quaternary heterocyclyl moiety of R³⁴ (rather than the quaternary heterocyclyl moiety of R⁶ as stated in the Office Action), is rendered moot by the cancellation of this claim. Moreover, claim 188, which has now been rewritten in independent form to include all of the limitations of canceled base claim 184, recites “PR¹³R¹⁴”, instead of “P¹³R¹⁴” to correct the typographical error noted in the Office Action.

Withdrawal of this rejection is respectfully requested.

t) In response to the rejection of claim 205 (rather than claim 185 as stated in the Office Action) and its dependent claims as being vague and indefinite for reciting “P⁹R¹⁰” in the list of substituents for the R³⁴ moieties (rather than the R⁶ moieties as stated in the Office Action), Applicants have amended claim 205 to replace “P⁹R¹⁰” with “PR⁹R¹⁰” and thereby correct the typographical error.

Withdrawal of this rejection is respectfully requested.

u) In response to the rejection of claim 205 (rather than claim 185 as stated in the Office Action) and its dependent claims as being vague and indefinite for reciting “P¹³R¹⁴” in the list of substituents for the quaternary heterocyclyl moiety of R³⁴ (rather than the quaternary heterocyclyl moiety of R⁶ as stated in the Office Action), Applicants have amended claim 205 to

replace “-P¹³R¹⁴” with “-PR¹³R¹⁴” and thereby correct the typographical error.

Withdrawal of this rejection is respectfully requested.

Rejection of Claims 163-166, 168-187, 189-204, 253, & 260 under 35 U.S.C. § 102(e)

Claims 163-166, 168-187, 189-204, 253, and 260 have been rejected under 35 U.S.C. § 102(e) as being anticipated by Frick *et al.* (U.S. Patent No. 6,227,831; hereinafter “Frick”).

In the interest of furthering prosecution, Applicants have canceled claims 163-166, 168-187, and 189-204. Claims 167 and 188 have been rewritten in independent form to include all limitations of the canceled base claims 163 and 184, respectively. Applicants have also amended multiple dependent claims 253 and 260 to preclude their dependency from cancelled claims 163-166, 168-187, and 189-204.

Withdrawal of this rejection is respectfully requested.

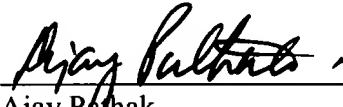
CONCLUSION

Accordingly, in view of the above amendments and remarks, this application is believed to be in condition for allowance, and a written indication of the same is respectfully requested.

Respectfully submitted,

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